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| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><i>(Use as many sheets as necessary)</i> |  |  |  | Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.<br><br><b>Complete if Known</b> |                                  |
|  |  |  |  | Application Number  | 10/596,945                       |
|  |  |  |  | Filing Date   | December 14, 2004                |
|  |  |  |  | First Named Inventor  | Susumu SHIOMI                    |
|  |  |  |  | Art Unit  | To be assigned                   |
|  |  |  |  | Examiner Name   | To be assigned /Phyllis Spivack/ |
| Sheet    1       of       1  |  |  |  | Attorney Docket Number  | 1089.060000/MAC/DJN              |

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| Examiner Signature | /Phyllis Spivack/ | Date Considered | 02/29/2008 |
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| <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b><br>(Use as many sheets as necessary) |        | Application Number       | 10/596,945           |
|   |        | Filing Date              | December 14, 2004    |
|   |        | First named Inventor     | Susumu SHIOMI        |
|   |        | Art Unit                 | To be assigned       |
|   |        | Examiner Name            | To be assigned       |
| Sheet   | 1 of 3 | Attorney Docket Number   | 1089.0600000/MAC/DJN |

| NON PATENT LITERATURE DOCUMENTS |                       |   |                |
|---------------------------------|-----------------------|---|----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published  | T <sup>2</sup> |
|                                 | NPL1                  | Furukawa, M., <i>et al.</i> , "Changes of Plasma Des-γ-Carboxy Prothrombin Levels in Patients With Hepatocellular Carcinoma in Response to Vitamin K," <i>Cancer</i> 69:31-38, J.B. Lippincott Company (1992)   |                |
|                                 | NPL2                  | Habu, D., <i>et al.</i> , "Role of Vitamin K <sub>2</sub> in the Development of Hepatocellular Carcinoma in Women With Viral Cirrhosis of the Liver," <i>JAMA</i> 292:358-361, American Medical Association (July 2004)   |                |
|                                 | NPL3                  | Ichida, F., <i>et al.</i> , "Clinical evaluation of human lymphoblastoid interferon (OPC-18) in patients with inactive chronic hepatitis C - A randomization study to find the optimal duration of treatment," <i>Kantansui</i> 32:101-127, ArcMedium (1996)  |                |
|                                 | NPL4                  | Ikeda, K. and Kumada, H., "Clinical significance of long-term natural course of and treatment of chronic hepatitis C liver disease," <i>Kanzo</i> 35:772-773, Nihon Kanzo Gakkai (1994)   |                |
|                                 | NPL5                  | Johnson, J.I., <i>et al.</i> , "Relationships between drug activity in NCI preclinical in vitro and in vivo models and early clinical trials," <i>Brit. J. Canc.</i> 84:1424-1431, Nature Publishing Group on behalf of Cancer Research UK (2001)   |                |
|                                 | NPL6                  | Koike, Y., <i>et al.</i> , "Des-γ-Carboxy Prothrombin As a Useful Predisposing Factor for the Development of Portal Venous Invasion in Patients with Hepatocellular Carcinoma," <i>Cancer</i> 91:561-569, John Wiley & Sons, Inc. (2001)  |                |
|                                 | NPL7                  | Koike, Y., <i>et al.</i> , "Randomized Prospective Study of Prevention from Tumor Invasion into Portal Vein in 120 Patients with Hepatocellular Carcinoma by Vitamin K Administration," available online at <a href="http://dw02.agora.com/planner/displayabstract.asp?presentationid=31">http://dw02.agora.com/planner/displayabstract.asp?presentationid=31</a> , Abstract ID 105864, 1 page (2002) |                |
|                                 | NPL8                  | Koike, Y., <i>et al.</i> , "A Randomized Prospective Controlled Study by Vitamin K-II Injection for the Purpose of Preventing Portal Venous Invasion (PVI)," <i>Kanzo</i> 43(suppl. 1):A64, abstract no. O-98, Nihon Kanzo Gakkai (2002)  | Yes            |
|                                 | NPL9                  | Unverified English language translation of Koike, Y., <i>et al.</i> , "A Randomized Prospective Controlled Study by Vitamin K-II Injection for the Purpose of Preventing Portal Venous Invasion (PVI)," <i>Kanzo</i> 43(suppl. 1):A64, abstract no. O-98, Nihon Kanzo Gakkai (2002)   |                |

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|   |   |    |   | Filing Date              | December 14, 2004    |
|   |   |    |   | First Named Inventor     | Susumu SHIOMI        |
|   |   |    |   | Art Unit                 | To be assigned       |
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| Sheet   | 2 | of | 3 | Attorney Docket Number   | 1089.0600000/MAC/DJN |

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|                                 | NPL10                 | Li, Z.-Q., et al., "Vitamin K uptake in hepatocytes and hepatoma cells," <i>Life Sci.</i> 70:2085-2100, Elsevier Science Inc. (2002)   |  |                |
|                                 | NPL11                 | Mizuta, T., et al., "A Clinical Study of the Effects of Vitamin K in Inhibiting Recurrence of Hepatocellular Carcinoma," <i>Jpn. J. Gastroenterol.</i> 99:A192, abstract no. 308, Gastroenterological Association of Japan (2002)  |  | Yes            |
|                                 | NPL12                 | Unverified English language translation of Mizuta, T., et al., "A Clinical Study of the Effects of Vitamin K in Inhibiting Recurrence of Hepatocellular Carcinoma," <i>Jpn. J. Gastroenterol.</i> 99:A192, abstract no. 308, Gastroenterological Association of Japan (2002) |  |                |
|                                 | NPL13                 | Mizuta, T., et al., "Inhibitory effect of vitamin K injection against the recurrence of hepatocellular carcinoma," <i>38<sup>th</sup> Annual Meeting of Liver Cancer Study Group of Japan</i> , pg. 135, abstract no. 110, (2002)  |  | Yes            |
|                                 | NPL14                 | Unverified English language translation of Mizuta, T., et al., "Inhibitory effect of vitamin K injection against the recurrence of hepatocellular carcinoma," <i>38<sup>th</sup> Annual Meeting of Liver Cancer Study Group of Japan</i> , pg. 135, abstract no. 110, (2002) |  |                |
|                                 | NPL15                 | Mizuta, T. and Yamamoto, K., "Vitamin K2 agent to inhibit recurrence of hepatic cancer," <i>J. Ther.</i> 83:1534-1535, Tokyo (April 2003)  |  |                |
|                                 | NPL16                 | Nishiguchi, S., et al., "Randomised trial of effects of interferon- $\alpha$ on incidence of hepatocellular carcinoma in chronic active hepatitis C with cirrhosis," <i>Lancet</i> 346:1051-1055, Lancet Publishing Group (1995)   |  |                |
|                                 | NPL17                 | Ohizumi, H., et al., "Geranylgeraniol Is a Potent Inducer of Apoptosis in Tumor Cells," <i>J. Biochem.</i> 117:11-13, Oxford University Press (1995)   |  |                |
|                                 | NPL18                 | O'Neil, J.M., et al., eds., "Vitamin K," in: <i>The Merck Index</i> , 13 <sup>th</sup> Ed., Merck & Co., Inc., Rahway, NJ, page 1787, item 10082, (2001)   |  |                |
|                                 | NPL19                 | Wang, Z., et al., "The Growth Inhibitory Effects of Vitamins K and Their Actions on Gene Expression," <i>Hepatology</i> 22:876-882, John Wiley & Sons, Inc. (1995)   |  |                |

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| Sheet   | 3 | of | 3                        | Attorney Docket Number | 1089.060000/MAC/DJN |

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|                                 | NPL20                 | Wu, F.Y.-H., <i>et al.</i> , "Comparison of Antitumor Activity of Vitamins K <sub>1</sub> , K <sub>2</sub> , and K <sub>3</sub> on Human Tumor Cells by Two (MTT and SRB) Cell Viability Assays," <i>Life Sci.</i> 52:1797-1804, Pergamon Press (1993) |  |                |
|                                 | NPL21                 | Yamaoka, Y., <i>et al.</i> , Liver Cancer Study Group of Japan, "Survey and Follow-up study of primary liver cancer in Japan, Report 14," <i>Kanzo</i> 41:799-810, Nihon Kanzo Gakkai (2000)   |  | Abs            |
|                                 | NPL22                 | English language abstract of Yamaoka, Y., <i>et al.</i> , Liver Cancer Study Group of Japan, "Survey and Follow-up study of primary liver cancer in Japan, Report 14," <i>Kanzo</i> 41:799-810, Nihon Kanzo Gakkai (2000)                              |  |                |
|                                 | NPL23                 | STN Database, Registry No. 863-61-6, "1,4-Naphthalenedione, 2-methyl-3-[(2E,6E,10E)-3,7,11,15-tetramethyl-2,6,10,14-hexadecatetraenyl]" (1984)   |  |                |
|                                 | NPL24                 | Copy of Russian Official Action for Russian Application No. 2004136304/15(039482), Russian Patent and Trademark Office, dated March 29, 2006   |  | Yes            |
|                                 | NPL25                 | Unverified English language translation of Russian Official Action for Russian Application No. 2004136304/15(039482), Russian Patent and Trademark Office, dated March 29, 2006  |  |                |
|                                 | NPL26                 | Patent Abstracts of Japan, English language abstract for JP 63-185921 (1988) .   |  |                |
|                                 | NPL27                 | Patent Abstracts of Japan, English language abstract for JP 06-305955 (1994) .   |  |                |
|                                 | NPL28                 | Dialog File 351, Accession No. 15924220, WPI English language abstract of WO 03/105819 (listed on accompanying PTO/SB/08A as document FP4) (2003) .  |  |                |
|                                 | NPL 29                | Copy of International Search Report for International Patent Application No. PCT/JP2004/018643, mailed April 19, 2005, Japanese Patent Office, Japan   |  |                |

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